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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

SRIVASTAVA, KAILASH C

ART UNIT PAPER NUMBER

1651

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application N .

10/010,227

Applicant(s)

HAMER ET AL.

Examiner

Dr. Kailash C. Srivastava

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on February 26, 2003 as Paper Number 7.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-49 is/are pending in the application.
- 4a) Of the above claim(s) 1-7, 12, 17 and 20-49 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 8-11, 13-16, 18 and 19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

1. Applicants' response filed February 26, 2003 as Paper Number 7 to election requirement in Office Action mailed February 07, 2003 as paper number 6 is acknowledged and entered.

### ***Restriction/Election***

2. Applicants' election **without** traverse of Group III, Claims 8-11, 13-16 and 18-19 filed February 26, 2003 as Paper Number 7 to election requirement in Office Action mailed February 7, 2003 as paper number 6 is acknowledged and entered. Since the election is made **without** traverse, the restriction requirement is deemed proper and is made FINAL.

Accordingly, Claims 1-7, 12, 17 and 20-49 are withdrawn from further consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. It is suggested that the non-elected claims be canceled in response to this Office action to expedite prosecution.

3. Claims 8-11, 13-16 and 18-19 are examined on merits.

### **Information Disclosure Statement**

4. Applicants' Information Disclosure (i.e., IDS) filed September 18, 2002 as paper number 5 has been made of record and considered.

### ***Claim Rejections - 35 U.S.C. § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

***The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.***

6. Claims 10-11 and 15-16 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to *Magnaporthe* 3-isopropylmalate dehydratase.

From the record of the present written disclosure, *Magnaporthe* is a fungus and is essential to the invention recited in those claims. Said *Magnaporthe* must therefore be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, failing to provide an enabling disclosure and failing to present the best mode contemplated by applicants for carrying out the invention without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological material. If the biological material is not so obtainable or available, a deposit of the microorganism (s) in a recognized depository may satisfy the requirements of 35 U.S.C. §112. Furthermore, in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, applicants may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

- (a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
- (b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
- (c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and
- (d) the deposit will be replaced if it should ever become inviable.

Applicant is directed to 37 CFR § 1.807 which states:

(b) A viability statement for each deposit of a biological material defined in paragraph (a) of this section not made under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure must be filed in the application and must contain:

- (1) The name and address of the depository;
- (2) The name and address of the depositor;
- (3) The date of deposit;
- (4) The identity of the deposit and the accession number given by the depository;
- (5) The date of the viability test;

(6) The procedures used to obtain a sample if the test is not done by the depository; and

(7) A statement that the deposit is capable of reproduction.

Applicant is also directed to 37 CFR § 1.809(d) which states:

(d) For each deposit made pursuant to these regulations, the specification shall contain:

(1) The accession number for the deposit;

(2) The date of the deposit.

7. Claims 18-19 are rejected under 35 U.S.C. § 112, first paragraph because from the record of the present written disclosure, those claims are non-enabling for the scope of that claim. The phrase "a polypeptide having at least 50% sequence identity with 3-isopropylmalate dehydratase at Lines 2-3 of Claims 18(a) and 19(a) is not enabling. Applicants have not disclosed where changes to the sequence can be made as claimed and still retain an active functional 3-isopropylmalate dehydratase, because it is not clear from the claim if the changes in the nucleotide sequence are allowed to change the polypeptide sequence? If the changes in the polynucleotide results in changes in the polypeptide, then Claim 18 is clearly non-enabled because it is not clearly supported in the specification how changes in the sequence by addition, deletion, substitution or insertion of amino acid residues will **not** change the structure and functionality of the polypeptide and therefore the 3-isopropylmalate dehydratase since from the current disclosure as presented the polypeptide is 3-isopropylmalate dehydratase.

An ordinary artisan would not be able to practice the invention because undue experimentation will be required to obtain the 3-isopropylmalate dehydratase activity cited *supra* due to the quantity of experimentation necessary; limited amount of guidance and limited number of working examples in the specification; nature of the invention; state of the prior art; relative skill level of those in the art; predictability or unpredictability in the art; and breadth of the claims. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

### ***Claim Rejections – 35 U.S.C. § 102***

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

***A person shall be entitled to a patent unless –***

**(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.**

9. Claims 8 and 13 are rejected under 35 U.S.C. §102(b) as anticipated by Bode et al., J. Basic Microbiology, 31(1), 1991, Pages 21-26.

Claims recite a method to identify an inhibitor of an enzyme, said enzyme is 3-isopropylmalate dehydratase.

Bode et al. teach a method to identify an inhibitor of 3-isopropylmalate dehydratase from *Candida maltosa* (Abstract, Lines 9-12) with both 2- isopropylmalate (i.e., alpha-isopropylmalate) and 3- isopropyl malate (i.e., beta-isopropylmalate) as substrates (Page 23, Lines 34-37). Please note that the prior art reference is also assaying for an inhibitor of same enzyme with same substrates involving the same steps as is recited in the claims and therefore, the prior art method (that of assaying inhibitors for 3-isopropylmalate dehydratase) inherently must function as claimed because said prior art method is assaying the same enzyme from patentably same genus, i.e. a fungus.

10. Claim 13 is rejected under 35 U.S.C. §102(b) as anticipated by Grandoni (U.S. Patent 5,998,420), with evidence from IUBMB Enzyme Nomenclature Classification (<http://www.chem.qmul.ac.uk/iubmb/enzyme/EC4/2/1/33.html>. Created 1972, modified, 1976, Page 1 of 1).

Claims recite a method to identify an inhibitor of an enzyme, said enzyme is 3-isopropylmalate dehydratase.

Grandoni teaches a method to identify an inhibitor of isopropylmalate isomerase, wherein beta- isopropylmalate is the substrate and the assay is conducted in presence of dimethylcitrate (Column 12, Lines 24-36) and further teaches that the inhibitors of said enzyme are known to be nitronates (See Figure 7 and Column 2, Lines 59-63). Please note that one of the synonym for 3-isopropylmalate dehydratase is isopropylmalate isomerase and both enzymes have the same enzyme classification number (See, IUBMB Enzyme Nomenclature Classification, <http://www.chem.qmul.ac.uk/iubmb/enzyme/EC4/2/1/33.html>. Created 1972, modified, 1976, Page 1 of 1). Please also note that the prior art reference is assaying for an inhibitor of same enzyme with same substrate (beta-isopropylmalate is 3-isopropylmalate) as is recited in the claims and therefore, the prior art method (that of assaying inhibitors for 3-isopropylmalate dehydratase) inherently must function as claimed

because said prior art method is comprised of same components and is being performed in the same way with same final result (that of identifying an inhibitor for 3-isopropylmalate dehydratase) as the claimed method (See e.g., In re Best, 195 USPQ 430, 433-CCPA 1977).

Therefore, the reference is deemed to anticipate the cited claims.

11. Claim 13 is rejected under 35 U.S.C. §102(b) as anticipated by Hawkes et al. (Z. Naturforsch, 1993, Volume 48c, Pages 364-368), with evidence from IUBMB Enzyme Nomenclature Classification (<http://www.chem.qmul.ac.uk/iubmb/enzyme/EC4/2/1/33.html>. Created 1972, modified, 1976, Page 1 of 1).

Claim recites a method to identify an inhibitor of 3-isopropylmalate dehydratase.

Hawkes et al. teach a method to identify an inhibitor of isopropylmalate isomerase, wherein beta- isopropylmalate is the substrate and the assay was conducted in presence of two different analogues (Figure 1, Page 364) of 1-NH<sub>2</sub>-2-nitrocyclopentane-1-carboxylic acid, a known leucine antimetabolite with plant growth regulating properties (Page 364, Column 1, Lines 32-36). The experimental results demonstrate that only the nitronate forms (i.e., analogues II and IV) inhibited the isopropylmalate isomerase significantly (Page 366, Column 2, Lines 13-16). Please note that one of the synonym for 3-isopropylmalate dehydratase is isopropylmalate isomerase and both enzymes have the same enzyme classification number (See, IUBMB Enzyme Nomenclature Classification, <http://www.chem.qmul.ac.uk/iubmb/enzyme/EC4/2/1/33.html>. Created 1972, modified, 1976, Page 1 of 1).

Therefore, the reference is deemed to anticipate the cited claims.

### ***Claim Rejections - 35 U.S.C. § 103***

12. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

***(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.***

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37

CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

13. Claims 8-9, 13-14 and 18-19 are rejected under 35 U.S.C. § 103 (a) as obvious over Bode et al (J. Basic Microbiology, 31(1), 1991, Pages 21-26), Grandoni (U.S. Patent 5,998,420), with evidence from IUBMB Enzyme Nomenclature Classification (<http://www.chem.qmul.ac.uk/iubmb/enzyme/EC4/2/1/33.html>). Created 1972, modified, 1976, Page 1 of 1) and Hawkes et al. (Z. Naturforsch, 1993, Volume 48c, Pages 364-368) in view of Rubin et al. (Gene, 1994, 140, Pages 131-135).

Claims recite a method to identify an inhibitor of an enzyme, said enzyme is a fungal 3-isopropylmalate dehydratase and said inhibitor is a candidate antibiotic. Furthermore, said enzyme is SEQ ID NO: 3 and is a polypeptide having at least 50% sequence homology and a polypeptide comprising at least 100 consecutive amino acids of a 3-isopropylmalate dehydratase.

Teachings from Bode et al., Grandoni and Hawkes et al. have been discussed *supra*.

None of the references cited *supra* teach a polypeptide of greater than 100 amino acids having a sequence homology of at least 50%.

Rubin et al. teach a polypeptide having 773 amino acids, said polypeptide having greater than 52% sequence homology to prokaryotic and eucaryotic (i.e., *Saccharomyces cerevisiae*)  $\alpha$ -isopropylmalate isomerases (Abstract, Lines 2-4, Page, 133, Column 1, Line 45 to Column 2, Line 2) as evidenced by searching nr database with BLAST algorithm and aligning the resulting homologs using the Clustal V Program (Page, 133, Column 1, Lines 41-45).

One having ordinary skill in the art would have been motivated to modify the teachings from Bode et al., Grandoni and Hawkes et al. references according to the teachings from Rubin et al. to search the nr database with BLAST algorithm and aligning the resulting homologs using the Clustal V Program, because all the three prior art references teach method to assay the same enzyme with same substrates and while all the three references (i.e., Bode et al., Grandoni and Hawkes et al.) teach methods to identify the inhibitors of said enzyme by a certain method, Rubin et al. teach assay for the same enzyme and also a method to determine a close homology of the amino acid sequence of



same enzyme from both prokaryotes and eucaryotes, wherein said eucaryotes are fungi. Thus, while teaching from Bode et al. reference (Lines 9-12) remedies the deficiency of a fungal 3-isopropylmalate dehydratase in teaching from Grandoni (Column 12, Lines 24-36; Figure 7 and Column 2, Lines 59-63), and teachings from Hawks et al. remedies the deficiency of identifying definite compounds (i.e., II and IV analogues of 1-NH<sub>2</sub>-2-nitrocyclopentane-1-carboxylic acid) as inhibitors for 3-isopropylmalate dehydratase (See, Figure 1, Page 364; Page 364, Column 1, Lines 32-36 and Page 366, Column 2, Lines 13-16) in teachings from Bode et al. and Grandoni; Rubin et al. remedy the deficiency of determining polypeptide sequence and sequence homology by teaching a method to search nr database with BLAST algorithm and aligning the resulting homologs using the Clustal V Program (Page, 133, Column 1, Lines 41-45)

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify teachings from Bode et al., Grandoni and Hawkes et al. references according to the teachings from Rubin et al. to identify an inhibitor of 3-isopropylmalate dehydratase, because each one of the prior art reference teaches a method to assay 3-isopropylmalate dehydratase and while Bode et al., Grandoni and Hawkes et al. teach methods to identify inhibitor of 3-isopropylmalate dehydratase, Rubin et al., remedy the deficiency in teachings of Bode et al., Grandoni and Hawkes et al., because Rubin et al. teach that the 773 amino acid polypeptide sequence is homologous to fungal and prokaryotic 3-isopropylmalate dehydratase.

From the teachings of the references cited *supra*, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

## Conclusion

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (703) 605-1196. The examiner can normally be reached on Monday-Thursday from 7:30 A.M. to 6:00 P. M. (Eastern Standard Time or Eastern Daylight Saving Time).

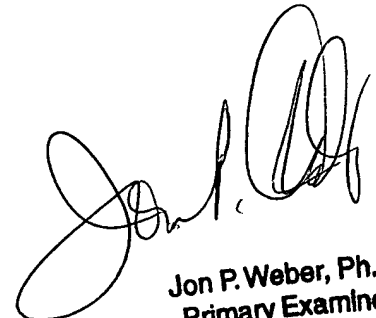
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743 Monday through

Thursday. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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May 19, 2003



Jon P. Weber, Ph.D.  
Primary Examiner